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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/699,966	11/03/2003	John Henry Kenten	100390-03578	5067
35745 7590 08/29/2007 KRAMER LEVIN NAFTALIS & FRANKEL LLP INTELLECTUAL PROPERTY DEPARTMENT 1177 AVENUE OF THE AMERICAS NEW YORK, NY 10036			EXAMINER MEAH, MOHAMMAD Y	
			ART UNIT 1652	PAPER NUMBER
			MAIL DATE 08/29/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/699,966	KENTEN ET AL.	
	Examiner	Art Unit	
	Mohammad Meah	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 April 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 124-180 is/are pending in the application.
- 4a) Of the above claim(s) 124-173, 177-180 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 174-176 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>11/3/03</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

With preliminary amendment of this application, the applicant, on date 04/30/2007 elected with traverse groups XVII (claims 174-176) for examination and cancelled claims 1-123.

Election/Restriction

During preliminary amendment of this application, the applicant, on date 04/30/2007 elected Group XVII (claims 174-176), drawn to Recombinant antibody comprising catalytic antibody comprising VL and antibody of VH region. Groups I- XVI and XVIII- XXIII (claims 177-181) of election/restriction-office action of date 11/01/2006 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to as non elected inventions.

Applicants arguments of 1.) that claims are grouped in different groups having same class and sub-class are improper and Applicants further argue that there would be no undue burden on the examiner to examine claims directed to different antibody and catalytic antibody conjugates. This is not persuasive because while the search for each of these distinct groups though are in same class and sub-class comprise different structures and would be overlapping it would not be coextensive. Art that applies for one conjugates having c different catalytic properties (conjugates comprise different class of biomolecules) may or may not be relevant to the others. Therefore the restriction is maintained.

Claim Rejection

35 USC 2nd Paragraph Rejection

The following is a quotation second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 174-175 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 174 is indefinite in the recitation of "further comprising a second single chain polypeptide" as claim does not previously (in claim 176) set forth "a first single chain polypeptide"

Claim 175 is indefinite in the recitation of "antibody is biospecific" as it is unclear how the antibody of claim 176 which comprises a single VH and VL region be bispecific.

35 USC 1st Paragraph written description Rejection

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 174-176 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a

Art Unit: 1652

way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 174-176 are directed to antibody conjugates comprising VH region of any antibody conjugated to VL region of any other antibody and further conjugation of thereof having any structure. The specification fails to describe in any fashion the physical and/or chemical properties of the claimed class of antibody or catalytic antibody.. Claimed class of antibody conjugate comprising VH and VL region comprise any protein molecule having any structure and function. Although VH region of an antibody comprise a less variant structure (most VH region of any antibody have defined structure) but VL region of an antibody has variable structure. Without any structural knowledge one skilled in art unable to make and use such antibody conjugate comprising VH region of any antibody conjugated to VL region of any other antibody. Furthermore no relationship between the antibody to any antigen in case of antibody and to any hapten molecule in the case of catalytic antibody is given. Production of specific antibody depends on the structure and nature of antigen and catalytic antibody depends on the structure of the specific transition state analog (Mader et al.). In most cases, even a single hapten molecule of a transition state analog (for forming or cleaving a bond) elicits multiple catalytic antibodies (Benkovic et al). Therefore, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed

Art Unit: 1652

invention. Therefore, one of skill in the art would not recognize that applicants' were in possession of the claimed invention.

Applicants' are referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

35 U.S.C. 112 first paragraph Enablement Rejections

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 174-176 are rejected under 35 U.S.C. 112, first paragraph are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for antibody VH region of monoclonal antibody B72.3 (specific to cancer) conjugated to VL region of a catalytic antibody (CAB) elicited against a phosphonate hapten for 5-fluorouridine 5-)-2,4,6 trimethylbenzine, does not reasonably provide enablement for any antibody conjugate comprising VH region of any antibody molecule conjugated to VL region of any antibody and further conjugate thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and for use the invention commensurate in scope with these claims.

Art Unit: 1652

Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breath of the claim(s).

These claims are so broad to encompass antibody conjugate comprising VH region of any antibody molecule conjugated to VL region of any antibody and further conjugate thereof. The antibody conjugates claimed herein comprising any molecule having any structure and any function. The specification discloses the structure and function of a few antigen and haptens and suggestion of eliciting antibodies and catalytic antibodies against them. The structure of the hapten and function is very crucial in antibody catalysis and production of specific catalytic antibody depends on the structure of the specific transition state analog. Production of antibody depends on the structure and function of the antigen. Finding a suitable transition state analog for any molecule and producing CAB for said reaction, and finding which among enormous number of variants of CAB has desired properties (catalyze said reaction) requires that one of ordinary skill in the art know or be provided with guidance for the selection of hapten to elicit suitable AB for production of CABs. Similarly to raise an antibody, one of ordinary skill in the art must know or be provided with guidance for the selection antigen to elicit antigenic reaction for the production of said

Art Unit: 1652

antibodies and in the instant case in order to produce chimeric antibodies as claimed, specific structural information about the VH and VL regions of the parent antibodies is needed as such chimeric antibodies can not be produced by immunization of a animal. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. This would clearly constitute **undue** experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has **not** been provided in the instant specification. Making a antibody conjugate comprising VH region of any antibody molecule conjugated to VL region of any catalytic antibody and further conjugate thereof without knowing the structure and function of corresponding antigen and hapten is unpredictable.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any conjugate comprising VH region of any antibody molecule conjugated to VL region of any catalytic antibody and further conjugate thereof. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of substances having the desired biological characteristics is

Art Unit: 1652

unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

CLAIM Rejection - 35 U.S.C 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
- (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
- (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 174-176 are rejected under 35 U.S.C. 102(b) as being anticipated by Novontny et al. (PNAS 1985, 82, 4592-4596). Novontny et al. teach antibody conjugates comprising VH region of one antibody fragment conjugated to VL region of another antibody fragment.

Claims 174-176 are rejected under 35 U.S.C. 102(b) as being anticipated by Scott et al. (J. Immun. 1989, 143, 293-298). Scott et al. teach antibody IgG comprising VH region of one antibody fragment conjugated to VL region of another antibody fragment.

Art Unit: 1652

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mohammad Meah whose telephone number is 571-272-1261. The examiner can normally be reached on 8:30-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


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Examiner, Art Unit 1652

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